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EXAMINER	
KUBELIK, ANNE R	
ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	07/827,906	BARTON ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____ .

DETAILED ACTION

1. Claims 27-44 are pending.

2. The terminal disclaimer filed on 21 November 2007 disclaiming the terminal portion of any patent granted on this application which would extend beyond (a) the period of abandonment of the application; or (b) the period extending beyond twenty years from the date on which the above-identified application was filed in the United States or, if the application contains a specific reference to an earlier filed application(s) under 35 U.S.C. 120, 121, or 365(c), from the date on which the earliest such application was filed has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 112

3. Claims 27-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is modified from the rejection set forth in the Office action mailed 25 February 2009. Applicant's arguments and the Baum Declaration, both filed 25 August 2009, have been fully considered but they are not persuasive.

Neither the instant specification nor the originally filed claims appear to provide support for modifying the codons for at least the first 25 amino acids in a coding sequence as in claims 28, 33 and 40. The specification only provides support for modifying "about 25 codons" at the N' terminal end of a coding sequence (pg 13, lines 15-22) and the original claims only provide

support for modifying "about 25 codons" at the N' terminal end of a coding sequence (claims 5 and 11).

Neither the instant specification nor the originally filed claims appear to provide support for substituting at least 59 amino acids in any coding sequence as in claim 29. The specification only provides support for modifying 59-138 codons of the Bt sequence used in the Examples (pg 13, line 9).

Thus, such claims constitute NEW MATTER. In response to this rejection, Applicant is required to point to support for the claims or to cancel the new matter.

Applicant urges that the rejection should not apply to claims 27, 30-32 and 38 (response pg 6).

This is not found persuasive because these claims encompass what is in the claims that depend from them. Thus, if there is new matter in a dependent claim, there is also new matter in the parent claim.

Applicant urges that additional codons beyond the first 25 or 59, that is at least 25 or 59, were contemplated; substituting codons in the remaining coding portion was taught in the specification pg 13, lines 11-16 (response pg 7-8).

This is not found persuasive because the sentence referring to as few as 59 amino acids refers to the Bt sequence used in the example. Further, 59-138 is not the same thing as at least 59; the latter includes substitutions of the first 139, or 140, or 141 amino acids, which are excluded by the former.

Applicant urges that the specification states that substitutions in as few as 59 codons at the 5' end enhances expression efficiency; one of skill in the art would understand the invention encompassed 59-138 substitutions at the 5' end (response pg 8).

This is not found persuasive because this statement refers specifically to the sequence in the examples, not to any coding sequence.

Applicant urges that the examples convey that substituting codons of at least the first 25 or 59 amino acids is part of the invention ; the examples have substitutions of the first 59, 104, and 138 codons and one of skill in the art would understand that it encompassed substituting the first 25 or 59 codons of a coding sequence (response pg 8).

This is not found persuasive because substitutions of the first 59, 104, and 138 codons apply only to the sequence in the examples. There is no support for "at least the first 25".

Applicant urges that one of skill in the art would understand that teaching to modify the 5' end, including the first 25 or 59 amino acids, is a general teaching not limited to a specific sequences in the examples, citing the Baum Declaration (response pg 9-10).

This is not found persuasive. The statements in the Declaration are addressed below.

The Declaration states that it would have been clear to a reader of the application that the specification conveys variations where the first 25 or about the first 25 codons are substituted (Declaration ¶3.2-3.3).

This is not found persuasive. "At least the first 25", not used by the specification, and "about 25", used by the specification, are not the same thing. The former encompasses the first

25 to the entire sequence. The second encompasses the first 23-27 or even 22-28 amino acids. These are not equivalent.

The Declaration states that the wording conveys that the inventors contemplated additional codons beyond the first 25; at least 25 is one definition of the invention (Declaration ¶3.4).

This is not found persuasive for the reasons above.

The Declaration states that substituting at least 59 codons at the 5' end was one definition. The excerpt had examples of as few as 59 and as many as 138 (Declaration ¶3.5).

This is not found persuasive because that excerpt was specially drawn to the sequence used in the examples, not to any coding sequence. Further, "at least 59" is not the same thing as "59-138 amino acids", as discussed above.

The Declaration states that it would have been clear to a scientist that the teachings to modify at least the first 25 or 59 amino acids applies to any sequence, quoting a portion of the specification (Declaration ¶3.8).

This is not found persuasive. While it is agreed that "about 25" apples to any coding sequence, as reflected in the altered rejection above, "59-138" applies to only the exemplified sequence; at least 59 apples to no sequence.

The Declaration states that the specification indicates that Bt endotoxin is an example of reduced heterologous gene expression in plants and that the invention is not limited to the example (Declaration ¶3.9).

This is not found persuasive because recitation of exact numbers of modifications, unless specified as applying to any sequence, only apply tot eh exemplified one.

The Declaration states that the modification of the first 25 or 59 amino acids is located just prior to the examples, which does not convey that the disclosure is limited to the sequence in the examples (Declaration ¶3.10).

This is not found persuasive because the paragraph states: "In the following example, the coding region of the protein expression cassette was altered by as few as 59 to as many as 138 codons, all at the amino terminal end of the protein or the 5' end of the coding region." (emphasis added). Thus, the paragraph, with respect to modifying 59 or 138 codons, refers to the nucleic acid in the example.

The Declaration states that original claim 10 confirms the modification of the 5' end apply to any coding sequence (Declaration ¶3.11).

This is found persuasive and this portion of the rejection is withdrawn. It is noted that original claim 11 recites that the modification at the 5'end is about 25 codons in length.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 27-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fischhoff et al (2003/0192078, which is a division of application 08/434,105). The rejection is repeated for the reasons of record as set forth in the Office action mailed 25 February 2009. Applicant's arguments filed 25 August 2009, have been fully considered but they are not persuasive.

The claims are drawn to a method of modifying a coding sequence by substituting codons used at the highest frequency in the instant Table 1.

On 12 December 1986 (see interference decision in the instant case mailed 29 January 2004), Fischhoff et al reduced to practice a method of designing a synthetic Bacillus thuringiensis endotoxin gene, said method comprising modifying the native sequence by substituting at least some of the codons in the native coding sequence with codons for the same amino acids but that have the highest frequency in plant genes, such as their Table I (¶54-56). Fischhoff et al also disclose attaching a promoter to the modified sequence (¶57-63).

Fischhoff et al do not teach the instant codon usage table.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of modifying codon usage in a gene to match that of the plant genome as taught by Fischhoff et al to use the codons that have the highest frequency in the instant table I. One of ordinary skill in the art would have been motivated to do so because which codons are determined to be at the highest frequency is determined by the genes used to make the codon usage table. The number of possible codons for each amino acid is limited; thus, there are a limited number of possible codon tables showing codons that have the highest frequency. Unless one such table provides unexpected results, each table is obvious over all the others. Substituting all the codons for those used at the highest frequency would be substituting at least the first 25 or at least 59 codons at the 5'end or codons at the 5' end.

Applicant urges that just because Fischhoff is prior art does not mean the instant invention is obvious in light of it (response pg 11).

This is not found persuasive because the instant invention is obvious in light of it for the reasons indicated.

Applicant urges that even in 1989 there would have been numerous combinations of gene sequences from which a person could select and sequence technologies would have enabled more; there is no reasoning defining the number of possible codon tables (response pg 12-13).

This is not found persuasive.

For the majority of amino acids (11 of the 18 for which there is more than one codon), the most frequency used codons in each of Fischhoff's table and the instant table are the same or are those for which there is only one possibility. Of those that differ (seven), the codons in the instant table use the second most commonly used (three) or the only other option (three) in Fischhoff's. Fischhoff's teaching to select codons to adjust the G+C content to about 50% (¶54) would prompt one of skill in the art to use some of these second most commonly used codons. Thus, the instant invention differs from Fischhoff's teachings in only a few codons; there would not have been a large number of different codons tables possible.

Applicant urges that there is no nexus between the observation of how codon tables are made and Applicant's specific one (response pg 13-14).

This is not found persuasive because unless one such table provides unexpected results, each table is obvious over all the others.

Double Patenting

6. Claims 27, 30-32, 38 and 41-44 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,833,449. The

rejection is repeated for the reasons of record as set forth in the Office action mailed 25 February 2009. Applicant's arguments and the Baum Declaration, both filed 25 August 2009, have been fully considered but they are not persuasive.

Although the conflicting claims are not identical, they are not patentably distinct from each other. A synthetic nucleic acid encoding a particular Cry endotoxin, wherein at least a portion of the coding sequence for the endotoxin exclusively uses the codons in the instant Fig 1 used at the highest frequency, as claimed in the issued patent, makes obvious a method of making a coding sequence for a Bt endotoxin using the codons in the instant Fig 1 used at the highest frequency, as claimed in the instant application. As the method steps are the same, methods of increasing the level of efficiency in expression of a Bt insecticidal protein are also made obvious. It would be obvious to one of skill in the art to attach regulatory sequences to the coding sequence, as expression in a plant requires plant regulatory sequences. Substituting all the codons for those used at the highest frequency would be substituting at least the first 25 or at least 59 codons at the 5'end or codons at the 5' end.

Applicant urges that the action fails to articulate why the nucleic acid anticipates or makes obvious the method (response pg 14-15).

This is not found persuasive because a nucleic acid made by selecting all its codons from those most used in Figure 1 is a species of all the nucleic acids made by a method of selecting codons from making a nucleic acid from those most used in Figure 1.

Applicant urges that *General Foods Corp. v. Studiengesellschaft Kohle mbH* makes clear that the disclosure of a patent cannot be used as prior art, even when the disclosure is in the claims (response pg 15).

This is not found persuasive. In *General Foods Corp. v. Studiengesellschaft Kohle mbH* the prior patent claim 1 had 9 steps; the first step was used as a basis for making a double patenting rejection. The decision states that a double patenting rejection must be based on all the method steps recited in a claim, not just one. That is not analogous to the instant case, where the species claimed in '449 is claimed reciting all the non-thought method steps of the instantly claimed method.

Applicant urges that '449 is directed to a nucleic acid, which is a chemical substance; it is not possible to determine from a nucleic acid the process by which is it made (response pg 15-16).

This is not found persuasive because in the instant case, the nucleic acid is defined by how it is made; the claim is not drawn to a sequence identifier, but to a nucleic acid made by selecting all its codons from those most frequently used in Fig. 1.

To make the nucleic acid claimed in '449, one of skill in the art must a) start with a coding sequence, that encoding a Cry1A protein of the Bacillus thuringiensis kurstaki subspecies HD-1, b) modify the coding sequence by substituting, for codons in the coding sequence, only codons for identical amino acids that have the highest frequency of use in plant genes, according to the plant codon usage table in Figure 1, and c) make a nucleic acid comprising the modified coding sequence that contains the substituted codons. In other words, one of skill in the art must practice a species of the instantly claimed invention. Thus, the nucleic acid of '449 makes obvious the instantly claimed method.

Conclusion

7. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, Ph.D., whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

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December 1, 2009

/Anne R Kubelik/
Primary Examiner, Art Unit 1638